

WHAT IS CLAIMED IS:

1           1.       A method for predicting the likelihood that a patient who is a candidate for  
2 treatment with an EGFR inhibitor will respond to said treatment, comprising determining  
3 the expression level of one or more prognostic RNA transcripts or their expression  
4 products in a cancer tissue sample obtained from said patient, wherein the prognostic  
5 transcript is the transcript of one or more genes selected from the group consisting of:  
6 STAT5A, STAT5B, WISP1, CKAP4, FGFR1, cdc25A, RASSF1, G-Catenin, H2AFZ,  
7 NME1, NRG1, BCL2, TAGLN, YB-1, Src, IGF1R, CD44, DIABLO, TIMP2, AREG,  
8 PDGFRa, CTSB, Hepsin, ErbB3, MTA1, Gus, and VEGF., wherein (a) over-expression  
9 of the transcript of one or more of STAT5A, STAT5B, WISP1, CKAP4, FGFR1,  
10 cdc25A, RASSF1, G-Catenin, H2AFZ, NME1, NRG1, BCL2, TAGLN, YB1, Src, IGF1R,  
11 CD44, DIABLO, TIMP2, AREG, PDGFRa, and CTSB, or the corresponding expression  
12 product, indicates that the patient is not likely to respond well to said treatment, and (b)  
13 over-expression of the transcript of one or more of Hepsin, ErbB3, MTA, Gus, and  
14 VEGF, or the corresponding expression product, indicates that the patient is likely to  
15 respond well to said treatment.

1           2.       The method of claim 1 comprising determining the expression level of at  
2 least two of said prognostic transcripts or their expression products.

1           3.       The method of claim 1 comprising determining the expression level of at  
2 least 5 of said prognostic transcripts or their expression products.

1           4.       The method of claim 1 comprising determining the expression level of all  
2 of said prognostic transcripts or their expression products.

1           5.       The method of claim 1 wherein over-expression is determined with  
2 reference to the mean expression level of all measured gene transcripts, or their  
3 expression products, in said sample.

1           6.       The method of claim 1 wherein said cancer is selected from the group  
2 consisting of ovarian cancer, colon cancer, pancreatic cancer, non-small cell lung cancer,  
3 breast cancer, and head and neck cancer.

1           7.       The method of claim 1 where the tissue is fixed, paraffin-embedded, or  
2 fresh, or frozen.

1           8.       The method of claim 1 where the tissue is from fine needle, core, or other  
2 types of biopsy.

1           9.       The method of claim 1 wherein the tissue sample is obtained by fine  
2 needle aspiration, bronchial lavage, or transbronchial biopsy.

1           10.      The method of claim 1 wherein the expression level of said prognostic  
2 RNA transcript or transcripts is determined by RT-PCR.

1           11.      The method of claim 1 wherein the expression level of said expression  
2 product or products is determined by immunohistochemistry.

1           12.      The method of claim 1 wherein the expression level of said expression  
2 product or products is determined by proteomics technology.

1           13.      The method of claim 1 wherein the assay for measurement of the  
2 prognostic RNA transcripts or their expression products is provided in the form of a kit or  
3 kits.

1           14.      The method of claim 1 wherein the EGFR inhibitor is an antibody or an  
2 antibody fragment.

1           15.      The method of claim 1 wherein the EGFR inhibitor is a small molecule.

1           16.      An array comprising polynucleotides hybridizing to the following genes:  
2 STAT5A, STAT5B, WISP1, CKAP4, FGFr1, cdc25A, RASSF1, G-Catenin, H2AFZ,  
3 NME1, NRG1, BCL2, TAGLN, YB1, Src, IGF1R, CD44, DIABLO, TIMP2, AREG,  
4 PDGFrA, CTSB, Hepsin, ErbB3, MTA, Gus, and VEGF, immobilized on a solid surface.

1           17.     An array comprising polynucleotides hybridizing to the following genes:  
2     STAT5A, STAT5B, WISP1, CKAP4, FGFR1, cdc25A, RASSF1, G-Catenin, H2AFZ,  
3     NME1, NRG1, BCL2, TAGLN, YB1, Src, IGF1R, CD44, DIABLO, TIMP2, AREG,  
4     PDGFRa, and CTSB.

1           18.     An array comprising polynucleotides hybridizing to the following genes:  
2     Hepsin, ErbB3, MTA, Gus, and VEGF.

1           19.     The array of any one of claims 6-18 wherein said polynucleotides are  
2     cDNAs.

1           20.     The array of claim 19 wherein said cDNAs are about 500 to 5000 bases  
2     long.

1           21.     The array of any one of claims 6-18 wherein said polynucleotides are  
2     oligonucleotides.

1           22.     The array of claim 21 wherein said oligonucleotides are about 20 to 80  
2     bases long.

1           23.     The array of claim 22 which comprises about 330,000 oligonucleotides.

1           24.     The array of any one or claims 6-18 wherein said solid surface is glass.

1           25.     A method of preparing a personalized genomics profile for a patient,  
2     comprising the steps of:

3           (a)     subjecting RNA extracted from cancer tissue obtained from the patient to  
4     gene expression analysis;

5           (b)     determining the expression level in the tissue of one or more genes  
6     selected from the group consisting of STAT5A, STAT5B, WISP1, CKAP4, FGFR1,  
7     cdc25A, RASSF1, G-Catenin, H2AFZ, NME1, NRG1, BCL2, TAGLN, YB1, Src, IGF1R,  
8     CD44, DIABLO, TIMP2, AREG, PDGFRA, CTSB, Hepsin, ErbB3, MTA, Gus, and  
9     VEGF, wherein the expression level is normalized against a control gene or genes and

10 optionally is compared to the amount found in a corresponding cancer reference tissue  
11 set; and  
12 (c) creating a report summarizing the data obtained by said gene expression  
13 analysis.

1 26. The method of claim 25 wherein said tissue is obtained from a fixed,  
2 paraffin-embedded biopsy sample.

1 27. The method of claim 26 wherein said RNA is fragmented.

1 28. The method of claim 25 wherein said report includes prediction of the  
2 likelihood that the patient will respond to treatment with an EGFR inhibitor.

1 29. The method of claim 25 wherein the cancer is lung cancer.

1 30. The method of claim 25 wherein the cancer is selected from the group  
2 consisting of colon cancer, head and neck cancer, lung cancer and breast cancer.

1 31. The method of claim 25 wherein said report includes recommendation for  
2 a treatment modality of said patient.

1 32. A method for amplification of a gene selected from the group consisting of  
2 STAT5A, STAT5B, WISP1, CKAP4, FGFR1, cdc25A, RASSF1, G-Catenin, H2AFZ,  
3 NME1, NRG1, BCL2, TAGLN, YB1, Src, IGF1R, CD44, DIABLO, TIMP2, AREG,  
4 PDGFRA, CTSB, Hepsin, ErbB3, MTA, Gus, and VEGF by polymerase chain reaction  
5 (PCR), comprising performing said PCR by using a corresponding amplicon listed in  
6 Table 3, and a corresponding primer-probe set listed in Table 4.

1 33. A PCR primer-probe set listed in Table 4.

1 34. A PCR amplicon listed in Table 3.

1           35.     A prognostic method comprising:  
2                 (a)     subjecting a sample comprising cancer cells obtained from a  
3 patient to quantitative analysis of the expression level of the RNA transcript of at least  
4 one gene selected from the group consisting of STAT5A, STAT5B, WISP1, CKAP4,  
5 FGFR1, cdc25A, RASSF1, G-Catenin, H2AFZ, NME1, NRG1, BCL2, TAGLN, YB1,  
6 Src, IGF1R, CD44, DIABLO, TIMP2, AREG, PDGFRa, and CTSC, or their product, and  
7                 (b)     identifying the patient as likely to have a decreased likelihood of  
8 responding well to treatment with an EGFR inhibitor if the normalized expression levels  
9 of said gene or genes, or their products, are elevated above a defined expression  
10 threshold.

1           36.     The method of claim 35 wherein said cancer cells are selected from the  
2 group consisting of non-small cell lung cancer (NSCLC) cells, colon cancer, head and  
3 neck cancer, lung cancer and breast cancer cells.

1           37.     A prognostic method comprising:  
2                 (a)     subjecting a sample comprising cancer cells obtained from a  
3 patient to quantitative analysis of the expression level of the RNA transcript of at least  
4 one gene selected from the group consisting of Hepsin, ErbB3, MTA, Gus, and VEGF, or  
5 their product, and  
6                 (b)     identifying the patient as likely to have an increased likelihood of  
7 responding well to treatment with an EGFR inhibitor if the normalized expression levels  
8 of said gene or genes, or their products, are elevated above a defined expression  
9 threshold.

1           38.     The method of claim 37 wherein said cancer cells are selected from the  
2 group consisting of non-small cell lung cancer (NSCLC) cells, colon cancer, head and  
3 neck cancer, lung cancer and breast cancer cells.

1           39.     The method of claim 35 or 37 wherein the levels of the RNA transcripts of  
2 said genes are normalized relative to the mean level of the RNA transcript or the product  
3 of two or more housekeeping genes.

1           40.     The method of claim 39 wherein the housekeeping genes are selected from  
2 the group consisting of glyceraldehyde-3-phosphate dehydrogenase (GAPDH), Cyp1,  
3 albumin, actins, tubulins, cyclophilin hypoxanthine phosphoribosyltransferase (HRPT),  
4 L32, 28S, and 18S.

1           41.     The method of claim 35 or 37 wherein the sample is subjected to global  
2 gene expression analysis of all genes present above the limit of detection.

1           42.     The method of claim 41 wherein the levels of the RNA transcripts of said  
2 genes are normalized relative to the mean signal of the RNA transcripts or the products of  
3 all assayed genes or a subset thereof.

1           43.     The method of claim 42 wherein the level of RNA transcripts is  
2 determined by quantitative RT-PCR (qRT-PCR), and the signal is a Ct value.

1           44.     The method of claim 43 wherein the assayed genes include at least 50  
2 cancer related genes.

1           45.     The method of claim 43 wherein the assayed genes includes at least 100  
2 cancer related genes.

1           46.     The method of claim 35 or 37 wherein said patient is human.

1           47.     The method of claim 46 wherein said sample is a fixed, paraffin-embedded  
2 tissue (FPET) sample, or fresh or frozen tissue sample.

1           48.     The method of claim 46 wherein said sample is a tissue sample from fine  
2 needle, core, or other types of biopsy.

1           49.     The method of claim 46 wherein said quantitative analysis is performed by  
2 qRT-PCR.

1           50.     The method of claim 46 wherein said quantitative analysis is performed by  
2 quantifying the products of said genes.

1           51.     The method of claim 50 wherein said products are quantified by  
2 immunohistochemistry or by proteomics technology.

1           52.     The method of claim 35 further comprising the step of preparing a report  
2 indicating that the patient has a decreased likelihood of responding to treatment with an  
3 EGFR inhibitor.

1           53.     The method of claim 37 further comprising the step of preparing a report  
2 indicating that the patient has an increased likelihood of responding to treatment with an  
3 EGFR inhibitor.

1           54.     A kit comprising one or more of (1) extraction buffer/reagents and  
2 protocol; (2) reverse transcription buffer/reagents and protocol; and (3) qPCR  
3 buffer/reagents and protocol suitable for performing the method of any one of claims 1,  
4 35 and 37.